Remarks:

With entry of this Amendment, Applicants add new claims 25 and 26. Applicants also cancel claims 2-5, 13, 14 and 17-24. Claims 7, 15 and 16 were previously cancelled. With this Amendment, claims 1, 6, 8-12, 25 and 26 are pending.

Rejection under 35 U.S.C. § 103(a) of Claims 1, 6 and 8-12

Claims 1, 6, and 8-12 stand rejected by the Office Action of November 5, 2008 ("the Office Action") under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 4,452,817 to Glen et al. (hereinafter "Glen") in view of U.S. Patent No. 7,166,303 to Meadows et al. ("Meadows").

Applicants respectfully submit that neither claim 1, as amended, nor claim 25 is taught or suggested by the Glen or Meadows references taken singly or in combination.

Amended claim 1 and new claim 25 recite a novel and non-obvious aqueous propofol formulation using Poloxamer 188 in combination with polyethylene glycol to form a composition that includes not more than 15% total excipients. The aqueous formulations recited by claims 1 and 25 are also substantially free of lipids.

In contrast, Glen teaches, at best, a propofol composition which includes 10 grams of propylene glycol (equating to 10.3% w/v)[1] in combination with 10 grams of Pluronic F68, also known as Poloxamer 188, (10.3 % w/v). (Glen column 7, lines 14-24.) Moreover, the total excipient content of Glen's described composition, the sum of the propylene glycol and the Poloxamer 188, is about 20.6%. This is well beyond the "not more than 15%" limit on excipients recited in claims 1 and 25. In fact, it is a feature of Applicants' invention as claimed that a propofol formulation suitable for injection can be achieved with minimal excipients. See paragraph 0023 of Applicants' disclosure as published.

Meadows likewise fails to teach or suggest Applicants' composition as claimed. Meadows is generally directed to aqueous propofol formulations. In particular, Meadows

[1] The formulation described by Glen is prepared by weight. Using reported densities for propylene glycol (1.03 g/mL), Poloxamer 188 (1.06 g/mL) and water (0.997 g/mL), it can be determined that the total volume of the preparation described by Glen is 97.3 mL. Accordingly, the w/v percentage of propylene glycol is (10 g/97.3mL) *100 = 10.3%. In the same way, Poloxamer 188 also accounts for 10.3% w/v.

teaches that Poloxamer 188 "only takes up 0.8% propofol in a 10% aqueous solution." (Meadows column 5, lines 6-7 and lines 61-63). To remedy the shortcomings Meadows professes for Poloxamer 188 as a propofol solvent, the only solution it provides is combining it with other poloxamers. For example, Meadows asserts that a combination of 3% Poloxamer 338 and 7% Poloxamer 188, solubilizes 1.8% propofol. (Meadows Example 7, Table 3 at column 12, line 50 to end of page). Applicants' invention as claimed is readily distinguishable from the Meadows reference because the amended claims expressly exclude substantive quantities of poloxamers other than Poloxamer 188. Moreover, Applicants' invention as claimed is further distinguishable from Meadows in that the amended claims expressly require polyethylene glycol. Meadows is entirely silent with respect to polyethylene glycol and so provides no teaching as to its use as an effective co-solvent with Poloxamer 188 for propofol. In fact, Meadows' only teaching with respect to additives other than poloxamers is limited to a brief discussion of tonicity modifiers, sterilizing agents, stabilizing agents, and bacteriostats. (See Meadows column 7, lines 42-65.)

In short, Glen and Meadows, taken singly or in combination, fail to teach a 1% propofol composition based on Poloxamer 188 that includes polyethylene glycol and has not more than 15% total excipients. Applicants respectfully submit that their invention is therefore distinguishable from the cited art. Inasmuch as Applicants' remaining claims depend from Claims 1 and 25 and incorporate each of their respective limitations, Applicants respectfully submit the dependent claims are also distinguishable from the cited art for at least this reason.

Obviousness-type Double Patenting:

Finally, the Office Action refers to the previous obviousness-type double patenting rejection of claims 1-6 and 8-14 as provisional because the co-pending application, 10/677,747, has not yet issued. Applicants will address this rejection, if needed, when the claims have been deemed otherwise allowable, application 10/677,747 has issued or been allowed, and this rejection has been made final.

Conclusion

For the reasons stated above, Applicants respectfully submit that the application as amended is in condition for allowance. A notice to this effect is respectfully requested. The Examiner is requested to telephone one of the Applicants' undersigned representatives if any further issues stand in the way of a Notice of Allowance.

Respectfully submitted,

5/2/08
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